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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WALICKA, MALGORZATA A	

ART UNIT	PAPER NUMBER
1652	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,514	BARR ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *3-7,9,10,12-15 and 18-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,11,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Requirement for Restriction filed on September 20, 2002, as paper 11, is acknowledged. Claims 1-35 are pending; claims 1, 2, 4, 8, 11, 16, and 17 are the subject of this Office Action. Claims 3, 5-7, 9-10, 12-15, 18-35 are withdrawn from consideration as directed to the non-elected invention.

Detailed Office Action

1. Restriction /Election

Applicant's election with traverse of Group I, claims 2, 4, 8 in part, and claims 11, 16, and 17, in paper No. 11 is acknowledged.

Applicants traverse that claim 1 should be joined to the present Group I. Claim 1 was inadvertently not included in Group I. The examiner includes claim 1 to Group I in examination on merits.

Furthermore, Applicants opinion is that Groups VIII and IX are method claims that incorporate all of the limitations of composition claims contained in Group I. If any of the claims of Group I is allowable the examiner will rejoin of method claims of Groups VIII and IX to the extent they incorporate all the limitations of allowed composition claims of Group I.

Applicants also request withdrawals of the restriction among Groups II, III and IV on the ground that they are classified in the same class and subclass, and represent combination/subcombination grouping. Applicants' arguments have been fully considered but they are moot in the light of election of Group I.

Claims 1, 2, 4, 8, 11, 16, and 17 are the subject of examination on merits. Claims 3, 5-7, 9-10, 12-15, 18-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Objections

Claim 8 is objected to under 37 CFR 1.75(c) as being in improper form because claim 8 is multiple dependent, as it depends on claims 1, 2, 3, or 4. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

3. Rejections

3.1. 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to protease inhibitors fragments comprising certain numbers of amino acid residues, without giving the sequence identification number from

which said fragments are taken. One skilled in the art would not know from which sequences to select amino acids 1- 394 or 1- 107

In addition, the term "about" in claims 4, 16 and 17 is a relative term, which renders the claims indefinite. The term "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. It is unknown which amino acid residues are included and which are excluded from the scope of the invention.

Claim 8 is rejected as dependent claim because it does not correct the language of the base claim 4.

3.2. 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.2.1. Lack of written description

Claims 1, 2 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to large and variable genera of fusion proteins.

Claim 1 is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof and

2) a second protease inhibitor or a functionally active portion hereof.

The scope of the claim encompasses a large genus of fusion proteins, which comprise an alpha 1-antitrypsin inhibitor and protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source. The genus encompasses fusion proteins that do not have the desired functional characteristics, i.e., they are not protease inhibitors, because the specification fails to teach a structure function relationship for the claimed fusion proteins. Applicants teach several representatives of the genus wherein the species have the function of protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8, 16, 10, 18, 14, 20 and 22. This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus of fusion proteins. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 2 is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof and

2) a secretory leukocytes protease inhibitor or a functionally active portion hereof.

The scope of the claim encompasses a large genus of fusion proteins that comprise an alpha 1-antitrypsin inhibitor and secretory leukocytes protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source. The genus encompasses fusion proteins that do not have the desired functional characteristics, i.e., they are not protease inhibitors.

The specification fails to teach a structure function relationship for the claimed components of the fusion proteins, therefore the structure of their active fragments is not taught. Applicants teach only two representatives of the genus wherein the species have the function of protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 11 is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof and

2) a serine protease inhibitor or a functionally active portion hereof.

The scope of the claim encompasses a large genus of fusion proteins that comprise an alpha 1-antitrypsin inhibitor and serine protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source. The genus encompasses fusion proteins that do not have the desired functional characteristics, i.e., they are not protease inhibitors.

The specification fails to teach a structure function relationship for the claimed components of the fusion proteins, therefore the structure of their active fragments is not taught. The specification teaches two inhibitors of serine proteases, alpha 1-antitrypsin whit the amino acid sequence of SEQ ID NO: 2, and secretory leukocyte protease inhibitor (SLPI), with the amino acid sequence of SEQ ID NO: 4), for which the functionally active fragments are defined.

The specification also fails to teach a structure function of the fusion proteins themselves. Applicants teach only two representatives of the genus wherein the species have the function of protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the

instant application was filed.

3.2.2. Scope of enablement

Claims 1, 2 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fusion proteins of SEQ ID NO: 8, 16, 10, 18, 14, 20 and 22, does not reasonably provide enablement for fusion proteins encompassing proteins consisting of:

1) protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof, and

2) a second protease inhibitor or a functionally active portion hereof, wherein the second protease inhibitor is:

a) any protease inhibitor,

b) any secretory leukocyte protease inhibitor,

c) any serine protease inhibitor.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the

nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any fusion protein comprising:

1) protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof and

2) a second protease inhibitor or a functionally active portion hereof, where in a second protease inhibitor is :

a) any protease inhibitor,

b) any secretory leukocyte protease inhibitor,

c) any serine protease inhibitor,

wherein the components of the fusion proteins originate from all natural and man-made sources.

Although the knowledge of production of fusion protein is well developed and skills of artisans high it is not possible for any person skilled in the art to make invention commensurate with the scope. The scope of the claims encompasses a large genera fusion proteins which comprise an alpha 1-antitrypsin inhibitor and protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source. The scope is so broad that it includes fusion proteins that have no desired fumctionlity of being a protease inhibitor.

Te specification fails to teach structure and function for all the claimed fusion proteins; see the above rejection for lack of written description. Therefore, to make the invention one skilled in the art has to construct an enormous number of DNA molecules encoding fusion proteins generally described in claims 1, 2 and 11, express them, examine the inhibitory action of the fusion proteins obtained and select the ones that have the desired function. Thus, the experimentation necessary to make the invention is out of the realm of routine experimentation.

The specification provides chemical structure for few fusion proteins that are inhibitors of proteases. They are called SLAPI, reverse SLAPI; TAPI, reverse TAPI; NTAPI and reverse NTAPI; S-linked TAPI, and are identified by SEQ ID NOs: 8, 16, 10, 18, 14, 20 and 22, respectively. Applicants also teach the recombinant production of SEQ ID NOs: 8, 16, 10, 18, 14, 20 and 22. However, the specification is not enabling for extremely large scope of molecules that may be components of the fused molecules of claimed invention. The genera of molecules listed under 1), 2) and (a), (b) and (c) above are not sufficiently described, as to their structure; see rejection for lack of written description. Without further guidance on the part of Applicants regarding the structure that ensures the desired characteristic of the fusion proteins, i.e., to have the capacity of inhibiting proteases, the probability of success in making the claimed invention is low, and experimentation left to those skilled in the art improperly extensive and undue.

4. Conclusion

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

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Art Unit 1652

Patent Examiner